Attorney Docket No.: **ISPH-0585**
Inventors: **Bennett et al.**
Serial No.: **09/918,186**
Filing Date: **July 30, 2001**
Page 2

REMARKS

Claims 1-15 are pending in the instant application. Claims 1-15 have been rejected. Claims 2-6 and 11-13 have been canceled. Reconsideration is respectfully requested in light of the following remarks.

I. Double Patenting

Claims 1 and 6-15 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-23 of U.S. Patent No. 6,335,194. The Examiner suggests that although the conflicting claims are not identical they are not patentably distinct from each other because of the scope of antisense oligonucleotide claimed and the scope of the claimed methods. Claims 7 and 8 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,165,788. The Examiner suggests that although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicants are filing herewith a terminal disclaimer under 37 CFR 1.130(b) with respect to both patents. Accordingly, withdrawal of these rejection is respectfully requested.

II. Rejection of Claims Under 35 U.S.C. 103(a)

Claim 6 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Altieri et al. (WO 98/22589) in view of Baracchini et al. (US Patent 5,801,154). The Examiner suggests that it would have been *prima facie* obvious for of ordinary skill in the art to use antisense oligonucleotides from 8 to 30 nucleobases in length to modulate apoptosis in cells since Altieri et al. have taught it would be desirable and contemplate using antisense to inhibit survivin while Baracchini teach design of such oligonucleotide in general.

Applicants have canceled claim 6, making this rejection moot. Accordingly, withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claims 1-15 have been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Examiner acknowledges that the specification as filed

is enabling for *in vitro* methods but then suggests that the specification as filed is not enabling for *in vivo* or therapeutic uses of the claimed compounds. The Examiner cites several articles on the technology of antisense to support the position regarding extrapolation to *in vivo* and pharmaceutical uses. Applicants respectfully traverse this rejection of the claims.

At the outset, Applicants respectfully point out that, as acknowledged by the Examiner, at pages 69-70 in Example 25 of the specification as filed, Applicants have provided *in vivo* animal data showing the pharmacological activity and demonstrating the efficacy of use of antisense compounds of the instant invention to inhibit IL-11-induced survivin expression. The Examiner suggests that the data provided do not show statistical significance, however, this is not an appropriate comment based on the type of data presented. The specification clearly states that the inventors report that there was no differences between the treated and control groups. This indicates that there was significant reduction of the expression of survivin. If that had not occurred, then the inventors would be reporting that controls and treated were not the same. This type of comparison of histological data, where the response was seen in 100% of the treated animals, is obviously statistically significant without applying such

statistical tests. Further, there is no requirement under 35 U.S.C. 112, first paragraph that statistical significance be shown. Therefore, the *in vivo* animal data provided in the specification as filed clearly demonstrates the *in vivo* pharmacological activity of the compounds of the instant invention and thus support the enablement of claims of the instant invention that are drawn to *in vivo* methods.

Additionally, Applicants disagree with the Examiner's suggestion that cited references support the position that application of antisense *in vivo* as a pharmaceutical is unpredictable.

The Examiner has pointed to two articles on the technology of antisense oligonucleotides to support the view that antisense technology is unpredictable. However, when one reads each of these papers as a whole, as required under MPEP 2141.02, these references actually teach the potential usefulness of this class of drugs in humans, and more importantly fail to provide any reasonable basis to doubt the pharmacological activity observed in cells and *in vivo* in animals in the instant invention would also occur in humans.

The paper by Jen and Gewirtz (2000) is a review paper on the evolution of technology to suppress gene expression, including

antisense technology, and its use in human disease. Nowhere does this paper teach or suggest that antisense compounds identified from well-designed *in vitro* studies and *in vivo* animal studies would be inherently unpredictable when used in humans *in vivo*.

The paper by Branch (1998) teaches the need to develop antisense molecules based on sound data and careful screening, such as is presented in the instant specification. Nowhere does the paper state that extrapolation from *in vitro* data and *in vivo* animal data to *in vivo* effects in humans is unpredictable.

Based on the presentation of *in vivo* animal data showing significant levels of pharmacological activity and the cancellation of the claims to method of treatment, withdrawal of the rejection is respectfully requested.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

Jane Massey Licata
Registration No. 32,257

Date: December 23, 2002

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, New Jersey 08053

(856) 810-1515